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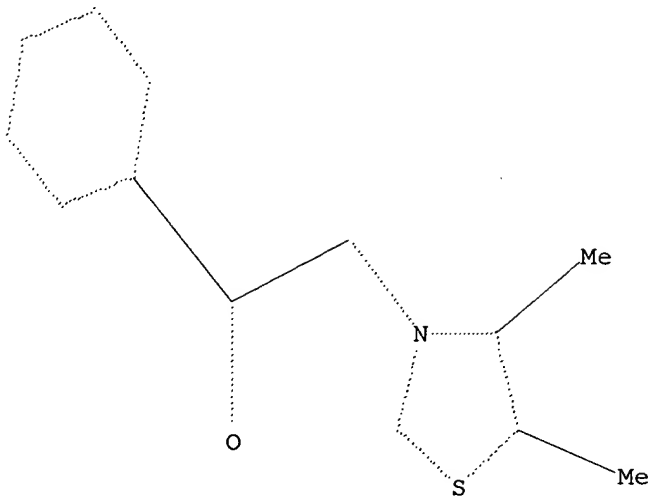

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L9 25687 SEA L8
L11 2 SEA L4 AND L9

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=> d his full

     (FILE 'HOME' ENTERED AT 16:27:23 ON 04 AUG 2005)

     FILE 'REGISTRY' ENTERED AT 16:27:31 ON 04 AUG 2005
L1              STRUCTURE UPLOADED
                D L1
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                D SCAN L2 1
L3           47 SEA SSS FUL L1

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L4           71 SEA L3
L5           63 DUP REM L4 (8 DUPLICATES REMOVED)
L6           18 SEA L5 AND (SYSTOL? OR HYPERTENS? OR DIASTOL? OR BLOOD(2A)
                PRESSUR? OR ANTIHYPERTENS? OR ANTI(W) HYPERTENS? OR VASCULAR(2A
                ) RESIST?)
L7            0 SEA L6 AND HYDROCHLOROTHIAZ?

     FILE 'REGISTRY' ENTERED AT 16:41:54 ON 04 AUG 2005
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L11           2 SEA L4 AND L9
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FILE 'HCAPLUS' ENTERED AT 16:42:33 ON 04 AUG 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE 'BIOSIS' ENTERED AT 16:42:33 ON 04 AUG 2005

FILE 'EMBASE' ENTERED AT 16:42:33 ON 04 AUG 2005

=> d his

(FILE 'HOME' ENTERED AT 16:27:23 ON 04 AUG 2005)

FILE 'REGISTRY' ENTERED AT 16:27:31 ON 04 AUG 2005
L1 STRUCTURE UPLOADED
L2 1 S L1 SSS SAM
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FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE' ENTERED AT 16:34:33 ON 04 AUG 2005
L4 71 S L3
L5 63 DUP REM L4 (8 DUPLICATES REMOVED)
L6 18 S L5 AND (SYSTOL? OR HYPERTENS? OR DIASTOL? OR BLOOD(2A)PRESSUR
L7 0 S L6 AND HYDROCHLOROTHIAZ?

FILE 'REGISTRY' ENTERED AT 16:41:54 ON 04 AUG 2005
E HYDROCHLOROTHIAZIDE/CN
L8 1 S E3

FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE' ENTERED AT 16:42:33 ON 04 AUG 2005

=> s l8
L9 25687 L8

=> s l6 and l9
L10 0 L6 AND L9

=> d l6 abs cbib kwic hitstr 1-18

L6 ANSWER 1 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
AB A review. Although the features of diabetic cardiomyopathy, atherosclerosis, and nephropathy have been clin. characterized, the pathogenesis and the mechanisms underlying the abnormalities in the diabetic heart and kidney are not fully understood. During the past several years, in an attempt to discover interventions for diabetes-related complications, researchers have refocused their attention from the hemodynamic aspects of the disease to the biochem. interactions of glucose and proteins. Diabetes is a disorder of chronic hyperglycemia, and glucose participates in diabetic complications such as atherosclerosis, cardiac dysfunction, and nephropathy. Chronic hyperglycemia accelerates the reaction between glucose and proteins and leads to the formation of advanced glycation end products (AGE), which form irreversible cross-links with many macromols. such as collagen. In

diabetes, these AGE accumulate in tissues at an accelerated rate. The development of the novel compound dimethyl-3-phenacylthiazolium chloride (alagebrium chloride), which chemical breaks AGE cross-links, led to several preclin. animal studies that showed an attenuation or reversal of disease processes of the heart and kidney. In diabetes, AGE not only structurally stiffen structural collagen backbones but also act as agonists to AGE receptors (RAGE) on various cell types, which stimulate the release of profibrotic growth factors, promote collagen deposition, increase inflammation, and ultimately lead to tissue fibrosis. In the heart, large vessels, and kidney, these reactions produce **diastolic** dysfunction, atherosclerosis, and renal fibrosis. Administration of the cross-link breaker alagebrium chloride in these diabetic animals attenuates these pathol. phenomena, restoring functionality to the heart, vasculature, and kidney.

2004:1089060 Document Number 143:4827 Importance of advanced glycation end products in diabetes-associated cardiovascular and renal disease. Cooper, Mark E. (Danielle Alberti Centre for Diabetic Complications, Wynn Domain, Vascular Division, Baker Heart Research Institute, Melbourne, Australia). American Journal of Hypertension, 17(12, Pt. 2), 31S-38S (English) 2004. CODEN: AJHYE6. ISSN: 0895-7061. Publisher: Elsevier Inc..

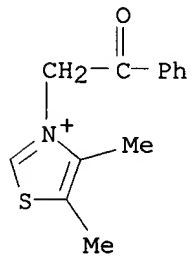
AB . . . collagen deposition, increase inflammation, and ultimately lead to tissue fibrosis. In the heart, large vessels, and kidney, these reactions produce **diastolic** dysfunction, atherosclerosis, and renal fibrosis. Administration of the cross-link breaker alagebrium chloride in these diabetic animals attenuates these pathol. phenomena,. . .

IT **341028-37-3**, Alagebrium chloride
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alagebrium chloride break AGE receptor agonist AGE cross links in chronic hyperglycemia, attenuates pathol. phenomena, restoring functionality of heart, vasculature and kidney in rat and mouse model)

IT **341028-37-3**, Alagebrium chloride
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alagebrium chloride break AGE receptor agonist AGE cross links in chronic hyperglycemia, attenuates pathol. phenomena, restoring functionality of heart, vasculature and kidney in rat and mouse model)

RN 341028-37-3 HCAPLUS

CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)-, chloride (9CI) (CA INDEX NAME)



● Cl^-

L6 ANSWER 2 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN

AB A review. Advanced glycation end product (AGE) formation that occurs with aging and diabetes leads to the crosslinking of proteins and subsequent changes in the physicochem. properties of tissues. Cellular responses to AGE that lead to either pathol. conditions or removal of AGE are mediated by a number of receptors that have been identified on various cell types such as macrophages, endothelial cells, and smooth-muscle cells. Mechanisms by which AGE affect the cardiovascular system include AGE crosslinking of long-lived proteins such as collagen and elastin and altered cellular responses. Alagebrium (3-phenacyl-4,5-dimethylthiazolium chloride, ALT-711) is the first drug in a new class of thiazolium therapeutic agents that break established AGE cross-links between proteins. In animal studies, alagebrium was effective in reducing large artery stiffness, slowing pulse-wave velocity, enhancing cardiac output, and improving left ventricular **diastolic** distensibility. In human studies to determine safety and efficacy, alagebrium was safe and well tolerated. In the first phase 2 clin. study, alagebrium improved arterial compliance in elderly patients with vascular stiffening. In two subsequent phase 2 clin. studies, one addressing **diastolic** heart failure and the other addressing **systolic hypertension**, alagebrium was effective in improving cardiac function and uncontrolled **systolic blood pressure**, particularly in more severely affected patients. Addnl. clin. studies to determine the utility of alagebrium in treating cardiovascular disorders associated with aging are in progress.

2004:1089059 Document Number 143:4826 Advanced glycation end-product cross-link breakers: A novel approach to cardiovascular pathologies related to the aging process. Bakris, George L.; Bank, Alan J.; Kass, David A.; Neutel, Joel M.; Preston, Richard A.; Oparil, Suzanne (Rush University Medical Center, Chicago, IL, USA). American Journal of Hypertension, 17(12, Pt. 2), 23S-30S (English) 2004. CODEN: AJHYE6. ISSN: 0895-7061. Publisher: Elsevier Inc..

AB . . . animal studies, alagebrium was effective in reducing large artery stiffness, slowing pulse-wave velocity, enhancing cardiac output, and improving left ventricular **diastolic** distensibility. In human studies to determine safety and efficacy, alagebrium was safe and well tolerated. In the first phase 2. . . study, alagebrium improved arterial compliance in elderly patients with vascular stiffening. In two subsequent phase 2 clin. studies, one addressing **diastolic** heart failure and the other addressing **systolic hypertension**, alagebrium was effective in improving cardiac function and uncontrolled **systolic blood pressure**, particularly in more severely affected patients. Addnl. clin. studies to determine the utility of alagebrium in treating cardiovascular disorders associated. . .

IT Glycoproteins
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(AGE (advanced glycosylation end product); phase 2 clin. study of alagebrium which break AGE cross-link between protein was effective, well tolerated in improving cardiac function by controlling **systolic blood pressure**, vascular stiffening, **hypertension** in elderly patient)

IT **Blood pressure**
Blood vessel, disease
Cardiovascular system, disease
Human
Hypertension

(phase 2 clin. study of alagebrium which break AGE cross-link between protein was effective, well tolerated in improving cardiac function by controlling **systolic blood pressure,** vascular stiffening, **hypertension** in elderly patient)

IT Diabetes mellitus
(phase 2 clin. study of alagebrium which break AGE cross-link formed in diabetes patient was effective, well tolerated in improving cardiac function by controlling **systolic blood pressure,** vascular stiffening, **hypertension**)

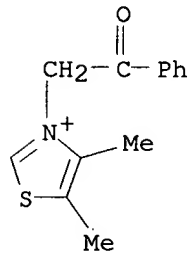
IT 28589-79-9, Thiazolium
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alagebrium class of thiazolium break AGE cross-link between protein was effective, well tolerated in improving cardiac function by controlling **systolic blood pressure,** vascular stiffening, **hypertension** in elderly patient)

IT **341028-37-3**, ALT-711
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phase 2 clin. study of ALT-711 which break AGE cross-link between protein was effective, well tolerated in improving cardiac function by controlling **systolic blood pressure,** vascular stiffening, **hypertension** in elderly patient)

IT **341028-37-3**, ALT-711
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phase 2 clin. study of ALT-711 which break AGE cross-link between protein was effective, well tolerated in improving cardiac function by controlling **systolic blood pressure,** vascular stiffening, **hypertension** in elderly patient)

RN 341028-37-3 HCAPLUS

CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)-, chloride (9CI) (CA INDEX NAME)



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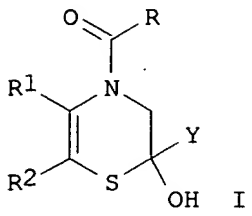
L6 ANSWER 3 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN

GI



I

AB The authors prepared thiazine compds. I [R = H, Me, HOCH2, MeCHOH; R1, R2 = H, C1-C6 alkyl, C1-C6 hydroxyalkyl, C3-C8 cycloalkyl, C1-C6 alkenyl, C1-C6 alkynyl, amino, monoalkylamino, dialkylaminoalkyl, pyrrolidin-1-ylalkyl; Y = C1-C6 alkyl, substituted and unsubstituted aryl; with the provisos that: (a) if Y = aryl, then at least one of R1 and R2 is other than H, and (b) if R2 = H, R1 = not Me] (and pharmaceutically acceptable salts thereof). For example, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)thiazolium chloride was reacted with NaOH to give I (R = H, R1 = R2 = Me, Y = Ph). The compds. are useful, among other things, as prodrugs which can be converted under acidic conditions to thiazolium agents. The compds. can be administered to mammals, including humans, for treatment of various indications including **hypertension**, reduced vascular compliance, **diastolic** dysfunction, heart failure, and isolated **systolic hypertension**.

2004:927187 Document Number 141:395566 Preparaton of dihydrothiazine prodrugs of thiazolium agents. Reinhard, Emily; Katten, Elliot (Alteon, Inc., USA). PCT Int. Appl. WO 2004094396 A2 20041104, 40 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US11984 20040416. PRIORITY: US 2003-PV463807 20030418; US 2004-824848 20040415.

AB . . . acidic conditions to thiazolium agents. The compds. can be administered to mammals, including humans, for treatment of various indications including **hypertension**, reduced vascular compliance, **diastolic** dysfunction, heart failure, and isolated **systolic hypertension**.

ST thiazine prepn prodrug thiazolium salt **hypertension** heart failure; vascular compliance reduced thiazine prodrug thiazolium salt

IT **Blood pressure**
(**diastolic**; preparation of dihydrothiazine prodrugs of thiazolium agents and their pharmaceutical use for **hypertension**, **diastolic** dysfunction, heart failure, and reduced vascular compliance)

IT Heart, disease
(failure; preparation of dihydrothiazine prodrugs of thiazolium agents and their pharmaceutical use for **hypertension**, **diastolic** dysfunction, heart failure, and reduced vascular compliance)

IT **Hypertension**
(preparation of dihydrothiazine prodrugs of thiazolium agents and their pharmaceutical use for **hypertension**, **diastolic** dysfunction, heart failure, and reduced vascular compliance)

IT Drug delivery systems
(prodrugs; preparation of dihydrothiazine prodrugs of thiazolium agents and their pharmaceutical use for **hypertension, diastolic** dysfunction, heart failure, and reduced vascular compliance)

IT **Blood pressure**
(**systolic**; preparation of dihydrothiazine prodrugs of thiazolium agents and their pharmaceutical use for **hypertension, systolic hypertension, diastolic** dysfunction, heart failure, and reduced vascular compliance)

IT Blood vessel, disease
(vascular compliance; preparation of dihydrothiazine prodrugs of thiazolium agents and their pharmaceutical use for **hypertension, diastolic** dysfunction, heart failure, and reduced vascular compliance)

IT 787621-17-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of dihydrothiazine prodrugs of thiazolium agents and their pharmaceutical use for **hypertension, diastolic** dysfunction, heart failure, and reduced vascular compliance)

IT 787621-19-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dihydrothiazine prodrugs of thiazolium agents and their pharmaceutical use for **hypertension, diastolic** dysfunction, heart failure, and reduced vascular compliance)

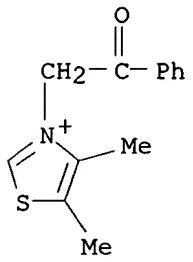
IT **341028-37-3** 787621-18-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of dihydrothiazine prodrugs of thiazolium agents and their pharmaceutical use for **hypertension, diastolic** dysfunction, heart failure, and reduced vascular compliance)

IT 356758-28-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of dihydrothiazine prodrugs of thiazolium agents and their pharmaceutical use for **hypertension, diastolic** dysfunction, heart failure, and reduced vascular compliance)

IT **341028-37-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of dihydrothiazine prodrugs of thiazolium agents and their pharmaceutical use for **hypertension, diastolic** dysfunction, heart failure, and reduced vascular compliance)

RN 341028-37-3 HCAPLUS

CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)-, chloride (9CI) (CA INDEX NAME)



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L6 ANSWER 4 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN

AB Background: Increased formation of advanced glycosylation end-products on body proteins is a consequence of aging and leads to exaggerated collagen crosslinking eventually increasing cardiovascular stiffness. This study reports our initial inquires into the cardiovascular and renal effects of a cross-link breaker (ALT-711) in aged spontaneously **hypertensive** rats (SHR). Methods and results: The first experiment, in 45-wk-old SHR, showed that (among four doses) the dose of 1 mg/kg/d of ALT-711 given for 4 mo was most effective in reducing left ventricular and aortic mass indexes. ALT-711 also reduced left ventricular hydroxyproline concentration (5.8±0.2 v 5.1±0.3 mg/g in controls, P <.05); however, it did not affect systemic or regional hemodynamics. In older SHR, ALT-711 (1 mg/kg/d) reduced (P <.05) **systolic** pressure (tail-cuff) (from 203±3 mm Hg at outset to 187±3 mm Hg at 8 wk). **Systolic** pressure remained unchanged in placebo-treated rats. In addition, left ventricular index (3.09±0.10 v 3.44±0.05 mg/g) and aortic mass index (1.54±0.04 v 1.74±0.05 mg/mm) were reduced by ALT-711. In the third experiment, 1-yr-old SHR were given vehicle or ALT-711 (1 mg/kg/d) or placebo until natural death. After 3 mo, ALT-711 markedly reduced urinary protein excretion (74.5±8.6 v 135.4±11.8 mg/24 h). Echocardiog. studies, performed at the outset and after 3 and 6 mo, revealed two changed indexes. Left ventricular end-**diastolic** diameter increased more in control than in ALT rats, whereas E-wave deceleration time decreased more in control than in ALT rats. Conclusions: Therapy with ALT-711 exerted beneficial cardiovascular and renal effects in aged SHR, improving **systolic** pressure, left ventricular mass, geometry, and hydroxyproline content while reducing urinary protein excretion.

2004:281528 Document Number 141:360381 Cardiovascular and renal effects of a collagen cross-link breaker (ALT 711) in adult and aged spontaneously **hypertensive** rats. Susic, Dinko; Varagic, Jasmina; Frohlich, Edward D. (Hypertension Research Laboratory, Ochsner Clinic Foundation, New Orleans, LA, USA). American Journal of Hypertension, 17(4), 328-333 (English) 2004. CODEN: AJHYE6. ISSN: 0895-7061. Publisher: Elsevier Science Inc..

TI Cardiovascular and renal effects of a collagen cross-link breaker (ALT 711) in adult and aged spontaneously **hypertensive** rats

AB . . . This study reports our initial inquires into the cardiovascular and renal effects of a cross-link breaker (ALT-711) in aged spontaneously **hypertensive** rats (SHR). Methods and results: The first experiment, in 45-wk-old SHR, showed that (among four doses) the dose of 1. . . P <.05); however, it did not affect systemic or regional hemodynamics. In

older SHR, ALT-711 (1 mg/kg/d) reduced (P <.05) **systolic** pressure (tail-cuff) (from 203±3 mm Hg at outset to 187±3 mm Hg at 8 wk). **Systolic** pressure remained unchanged in placebo-treated rats. In addition, left ventricular index (3.09±0.10 v 3.44±0.05 mg/g) and aortic mass index (1.54±0.04. . . mg/24 h). Echocardiog. studies, performed at the outset and after 3 and 6 mo, revealed two changed indexes. Left ventricular end-**diastolic** diameter increased more in control than in ALT rats, whereas E-wave deceleration time decreased more in control than in ALT rats. Conclusions: Therapy with ALT-711 exerted beneficial cardiovascular and renal effects in aged SHR, improving **systolic** pressure, left ventricular mass, geometry, and hydroxyproline content while reducing urinary protein excretion.

ST collagen cross link breaker cardiovascular renal system hemodynamics **hypertension**

IT Glycoproteins
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(AGE (advanced glycosylation end product); collagen cross-linker ALT 711 effectively reduced left ventricular and aortic indexes, left ventricular hydroxy proline content, **systolic** pressure, proteinuria, left ventricular **diastolic** diameter, E-wave deceleration in aged SHR)

IT Artery, disease
(aorta, stiffness; collagen cross-linker ALT 711 effectively reduced left ventricular and aortic indexes, left ventricular hydroxy proline content, **systolic** pressure, proteinuria, left ventricular **diastolic** diameter, E-wave deceleration in aged SHR)

IT Artery
(aorta; collagen cross-linker ALT 711 effectively reduced left ventricular and aortic indexes, left ventricular hydroxy proline content, **systolic** pressure, proteinuria, left ventricular **diastolic** diameter, E-wave deceleration in aged SHR)

IT Cardiovascular system
Circulation
(collagen cross-linker ALT 711 effectively reduced left ventricular and aortic indexes, left ventricular hydroxy proline content, **systolic** pressure, left ventricular **diastolic** diameter, E-wave deceleration in aged SHR)

IT Aging, animal
Cardiovascular agents
Heart
(collagen cross-linker ALT 711 effectively reduced left ventricular and aortic indexes, left ventricular hydroxy proline content, **systolic** pressure, proteinuria, left ventricular **diastolic** diameter, E-wave deceleration in aged SHR)

IT Collagens, biological studies
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(crosslinked; collagen cross-linker ALT 711 effectively reduced left ventricular and aortic indexes, left ventricular hydroxy proline content, **systolic** pressure, proteinuria, left ventricular **diastolic** diameter, E-wave deceleration in aged SHR)

IT Heart
(left ventricle; collagen cross-linker ALT 711 effectively reduced left ventricular and aortic indexes, left ventricular hydroxy proline content, **systolic** pressure, proteinuria, left ventricular **diastolic** diameter, E-wave deceleration in aged SHR)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proteinuria; collagen cross-linker ALT 711 effectively reduced left ventricular and aortic indexes, left ventricular hydroxy proline content, **systolic** pressure, proteinuria, left ventricular **diastolic** diameter, E-wave deceleration in aged SHR)

IT **Hypertension**
(spontaneous; collagen cross-linker ALT 711 effectively reduced left ventricular and aortic indexes, left ventricular hydroxy proline content, **systolic** pressure, proteinuria, left ventricular **diastolic** diameter, E-wave deceleration in aged SHR)

IT Heart
(toxicity; collagen cross-linker ALT 711 effectively reduced left ventricular and aortic indexes, left ventricular hydroxy proline content, **systolic** pressure, proteinuria, left ventricular **diastolic** diameter, E-wave deceleration in aged SHR)

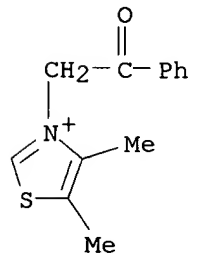
IT 51-35-4, Hydroxyproline
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(collagen cross-linker ALT 711 effectively reduced left ventricular and aortic indexes, left ventricular hydroxy proline content, **systolic** pressure, proteinuria, left ventricular **diastolic** diameter, E-wave deceleration in aged SHR)

IT **181069-80-7**, ALT 711
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(collagen cross-linker ALT 711 effectively reduced left ventricular and aortic indexes, left ventricular hydroxy proline content, **systolic** pressure, proteinuria, left ventricular **diastolic** diameter, E-wave deceleration in aged SHR)

IT **181069-80-7**, ALT 711
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(collagen cross-linker ALT 711 effectively reduced left ventricular and aortic indexes, left ventricular hydroxy proline content, **systolic** pressure, proteinuria, left ventricular **diastolic** diameter, E-wave deceleration in aged SHR)

RN 181069-80-7 HCAPLUS

CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)-, bromide (9CI) (CA INDEX NAME)



● Br^-

L6 ANSWER 5 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN

AB Aging and diabetes mellitus (DM) both affect the structure and function of the myocardium, resulting in increased collagen in the heart and reduced cardiac function. As part of this process, hyperglycemia is a stimulus for the production of advanced glycation end products (AGEs), which covalently modify proteins and impair cell function. The goals of this study were first to examine the combined effects of aging and DM on hemodynamics and collagen types in the myocardium in 12 dogs, 9-12 yr old, and second to examine the effects of the AGE crosslink breaker phenyl-4,5-dimethylthazolium chloride (ALT-711) on myocardial collagen protein content, aortic stiffness, and left ventricular (LV) function in the aged diabetic heart. The alloxan model of DM was utilized to study the effects of DM on the aging heart. DM induced in the aging heart decreased LV **systolic** function (LV ejection fraction fell by 25%), increased aortic stiffness, and increased collagen type I and type III protein content. ALT-711 restored LV ejection fraction, reduced aortic stiffness and LV mass with no reduction in blood glucose level (199±17 mg/dL), and reversed the upregulation of collagen type I and type III. Myocardial LV collagen solubility (%) increased significantly after treatment with ALT-711. These data suggest that an AGE crosslink breaker may have a therapeutic role in aged patients with DM.

2004:1425 Document Number 140:91894 Glycation end-product cross-link breaker reduces collagen and improves cardiac function in aging diabetic heart. Liu, Jing; Masurekar, Malthi R.; Vatner, Dorothy E.; Jyothirmayi, Garikiparthy N.; Regan, Timothy J.; Vatner, Stephen F.; Meggs, Leonard G.; Malhotra, Ashwani (Department of Cell Biology and Molecular Medicine, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, NJ, 07101, USA). American Journal of Physiology, 285(6, Pt. 2), H2587-H2591 (English) 2003. CODEN: AJPHAP. ISSN: 0002-9513. Publisher: American Physiological Society.

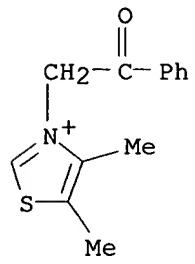
AB . . . . was utilized to study the effects of DM on the aging heart. DM induced in the aging heart decreased LV **systolic** function (LV ejection fraction fell by 25%), increased aortic stiffness, and increased collagen type I and type III protein content.. . .

IT **341028-37-3**, ALT-711
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glycation end-product crosslink breaker reduces collagen and improves cardiac function in aging diabetic heart)

IT **341028-37-3**, ALT-711
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glycation end-product crosslink breaker reduces collagen and improves cardiac function in aging diabetic heart)

RN 341028-37-3 HCAPLUS

CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)-, chloride (9CI) (CA INDEX NAME)



● Cl^-

L6 ANSWER 6 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN

AB A review. Long-lived structural proteins, collagen and elastin, undergo continual non-enzymic crosslinking during aging and in diabetic individuals. This abnormal protein crosslinking is mediated by advanced glycation end products (AGEs) generated by non-enzymic glycosylation of proteins by glucose. The AGE-derived protein crosslinking of structural proteins contributes to the complications of long-term diabetes such as nephropathy, retinopathy, and neuropathy. AGE-crosslinks have also been implicated in age-related cardiovascular diseases. Potential treatment strategies for these AGE-derived complications include prevention of AGE-formation and breaking of the existing AGE-crosslinks. The therapeutic potential of the AGE-inhibitor, pimagedine (aminoguanidine), has been extensively investigated in animal models and in Phase 3 clin. trials. This review presents the pre-clin. and clin. studies using ALT-711, a highly potent AGE-crosslink breaker that has the ability to reverse already-formed AGE-crosslinks. Oral administration of ALT-711 has resulted in a rapid improvement in the elasticity of stiffened myocardium in exptl. animals. Topical administration of ALT-711 was effective in improving the skin hydration of aged rats. The therapeutic potential of crosslink breakers for cardiovascular complications and dermatol. alterations associated with aging and diabetes is discussed.

2003:804088 Document Number 140:121913 Therapeutic potential of breakers of advanced glycation end product-protein crosslinks. Vasan, Sara; Foiles, Peter; Founds, Hank (Alteon Inc., Ramsey, NJ, 07446, USA). Archives of Biochemistry and Biophysics, 419(1), 89-96 (English) 2003. CODEN: ABBIA4. ISSN: 0003-9861. Publisher: Elsevier Science.

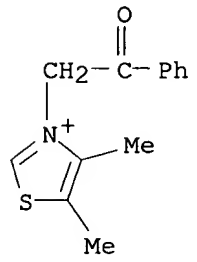
IT Aging, animal
Antihypertensives
Diabetes mellitus
Human
Hypertension
(therapeutic potential of AGE crosslink breakers)

IT **341028-37-3**, ALT 711
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALT 711; therapeutic potential of AGE crosslink breakers)

IT **341028-37-3**, ALT 711
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALT 711; therapeutic potential of AGE crosslink breakers)

RN 341028-37-3 HCAPLUS

CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)-, chloride (9CI) (CA INDEX NAME)



L6 ANSWER 7 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN

AB Renal accumulation of advanced glycation end products (AGEs) has been linked to the progression of diabetic nephropathy. Cleavage of pre-formed AGEs within the kidney by a cross-link breaker, such as ALT-711, may confer renoprotection in diabetes. STZ diabetic rats were randomized into (a) no treatment (D); (b) treatment with the AGE cross-link breaker, ALT-711, weeks 16-32 (DALT early); and (c) ALT-711, weeks 24-32 (DALT late). Treatment with ALT-711 resulted in a significant reduction in diabetes-induced serum and renal AGE peptide fluorescence, associated with decreases in renal carboxymethyllysine and RAGE immunostaining. Crosslinking of tail tendon collagen seen in diabetic groups was attenuated only by 16 wk of ALT-711 treatment. ALT-711, independent of treatment duration, retarded albumin excretion rate (AER), reduced **blood pressure**, and renal hypertrophy. It also reduced diabetes-induced increases in gene expression of transforming growth factor β1 (TGF-β1), connective tissue growth factor (CTGF), and collagen IV. However, glomerulosclerotic index, tubulointerstitial area, total renal collagen, nitrotyrosine, protein expression of collagen IV, and TGF-β1 only showed improvement with early ALT treatment alone. This study demonstrates the utility of a cross-link breaker as a treatment for diabetic nephropathy and describes effects not only on renal AGEs but on putative mediators of renal injury, such as prosclerotic cytokines and oxidative stress.

2003:730751 Document Number 139:301751 The breakdown of pre-existing advanced glycation end products is associated with reduced renal fibrosis in experimental diabetes. Forbes, Josephine M.; Thallas, Vicki; Thomas, Merlin C.; Founds, Hank W.; Burns, Wendy C.; Jerums, George; Cooper, Mark E. (Division of Diabetic Complications, Baker Medical Research Institute, Melbourne, 8008, Australia). FASEB Journal, 17(12), 1762-1764, 10.1096/fj.02-1102fje (English) 2003. CODEN: FAJOEC. ISSN: 0892-6638. Publisher: Federation of American Societies for Experimental Biology.

AB . . . was attenuated only by 16 wk of ALT-711 treatment. ALT-711, independent of treatment duration, retarded albumin excretion rate (AER), reduced **blood pressure**, and renal hypertrophy. It also reduced diabetes-induced increases in gene expression of transforming growth factor β1 (TGF-β1), connective tissue growth. . .

IT **Hypertension**

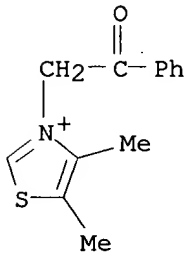
Hypertrophy
(renal, reduction by cross-link breaker ALT-711; breakdown of pre-existing advanced glycation end products is associated with reduced renal fibrosis in exptl. diabetes)

IT **341028-37-3**, ALT 711
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALT 711; breakdown of pre-existing advanced glycation end products is associated with reduced renal fibrosis in exptl. diabetes)

IT **341028-37-3**, ALT 711
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALT 711; breakdown of pre-existing advanced glycation end products is associated with reduced renal fibrosis in exptl. diabetes)

RN 341028-37-3 HCAPLUS

CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)-, chloride (9CI) (CA INDEX NAME)



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L6 ANSWER 8 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN

AB The invention provides a method of treating, ameliorating, or preventing certain fibrotic diseases or other indications in an animal, including a human, comprising administering an effective amount of a heterocyclic compound The effect of 3-(2-phenyl-2-oxoethyl)-4,5-dimethylthiazolium salt in a rat heart infarction model is presented.

2002:521411 Document Number 137:73284 Method using heterocyclic compounds for treating fibrotic diseases or other indications. Wagle, Dilip; Gall, Martin; Bell, Stanely C.; Lavoie, Edmond J. (Alteon, Inc., USA). PCT Int. Appl. WO 2002053101 A2 20020711, 60 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US50824 20011228. PRIORITY: US 2000-2000/PV25942U 20001229; US 2001-2001/PV25925U 20010102; US 2001-2001/PV296256 20010606.

IT Alzheimer's disease
Anti-Alzheimer's agents

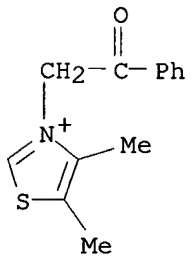
Antiarteriosclerotics
Antiarthritics
Antiasthmatics
Antidiabetic agents
Antihypertensives
Antitumor agents
Arteriosclerosis
Asthma
Atherosclerosis
Cardiovascular agents
Cataract
Diabetes mellitus
Dialysis
Fibrosis
Human
Hypertension
Nervous system agents
Osteoarthritis
Periodontium, disease
Rheumatoid arthritis
Sickle cell anemia
(heterocyclic compds. for treatment of fibrotic diseases or other conditions)

IT **Blood pressure**
(**systolic, systolic hypertension;**
heterocyclic compds. for treatment of fibrotic diseases or other conditions)

IT **393121-34-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heterocyclic compds. for treatment of fibrotic diseases or other conditions)

IT **393121-34-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heterocyclic compds. for treatment of fibrotic diseases or other conditions)

RN 393121-34-1 HCAPLUS
CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 9 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
AB Arterial stiffening with increased pulse pressure is a leading risk factor for cardiovascular disease in the elderly. We tested whether ALT-711, a novel nonenzymic breaker of advanced glycation end-product crosslinks,

selectively improves arterial compliance and lowers pulse pressure in older individuals with vascular stiffening. Nine US centers recruited and randomly assigned subjects with resting arterial pulse pressures >60 mm Hg and **systolic** pressures >140 mm Hg to once-daily ALT-711 (210 mg; n=62) or placebo (n=31) for 56 days. Preexisting **antihypertensive** treatment (90% of subjects) was continued during the study. Morning upright **blood pressure**, stroke volume, cardiac output, systemic **vascular resistance**, total arterial compliance, carotid-femoral pulse wave velocity, and drug tolerability were assessed. ALT-711 netted a greater decline in pulse pressures than placebo (-5.3 vs. -0.6 mm Hg at day 56; P=0.034 for treatment effect by repeated-measures ANOVA). **Systolic** pressure declined in both groups, but **diastolic** pressure fell less with ALT-711 (P=0:056). Mean pressure declined similarly in both groups (-4 mm Hg; P<0.01 for each group, P=0.34 for treatment effect). Total arterial compliance rose 15% in ALT-711-treated subjects vs. no change with placebo (P=0.015 vs. ALT-711), an effect that did not depend on reduced mean pressure. Pulse wave velocity declined 8% with ALT-711 (P<0.05 at day 56, P=0.08 for treatment effect). Systemic arterial resistance, cardiac output, and heart rate did not significantly change in either group. ALT-711 improves total arterial compliance in aged humans with vascular stiffening, and it may provide a novel therapeutic approach for this abnormality, which occurs with aging, diabetes, and isolated **systolic hypertension**.

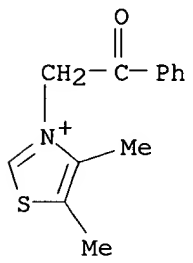
2001:783968 Document Number 136:112431 Improved arterial compliance by a novel advanced glycation end-product crosslink breaker. Kass, David A.; Shapiro, Edward P.; Kawaguchi, Miho; Capriotti, Anne R.; Scuteri, Angelo; deGroof, Robert C.; Lakatta, Edward G. (Division of Cardiology, The Johns Hopkins Medical Institutions, Baltimore, MD, 21287, USA). Circulation, 104(13), 1464-1470 (English) 2001. CODEN: CIRCAZ. ISSN: 0009-7322. Publisher: Lippincott Williams & Wilkins.

AB . . . with vascular stiffening. Nine US centers recruited and randomly assigned subjects with resting arterial pulse pressures >60 mm Hg and **systolic** pressures >140 mm Hg to once-daily ALT-711 (210 mg; n=62) or placebo (n=31) for 56 days. Preexisting **antihypertensive** treatment (90% of subjects) was continued during the study. Morning upright **blood pressure**, stroke volume, cardiac output, systemic **vascular resistance**, total arterial compliance, carotid-femoral pulse wave velocity, and drug tolerability were assessed. ALT-711 netted a greater decline in pulse pressures than placebo (-5.3 vs. -0.6 mm Hg at day 56; P=0.034 for treatment effect by repeated-measures ANOVA). **Systolic** pressure declined in both groups, but **diastolic** pressure fell less with ALT-711 (P=0:056). Mean pressure declined similarly in both groups (-4 mm Hg; P<0.01 for each group,. . . vascular stiffening, and it may provide a novel therapeutic approach for this abnormality, which occurs with aging, diabetes, and isolated **systolic hypertension**.

IT **181069-80-7**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALT 711; improved arterial compliance by a novel advanced glycation end-product crosslink breaker)

IT **181069-80-7**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALT 711; improved arterial compliance by a novel advanced glycation end-product crosslink breaker)

RN 181069-80-7 HCAPLUS
CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)-, bromide (9CI) (CA INDEX NAME)



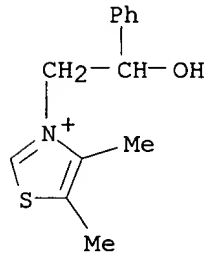
L6 ANSWER 10 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN
AB A method and compns. are disclosed for improving the elasticity or reducing wrinkles of the skin, treating disorders such as diabetes or treating or preventing adverse sequelae of diabetes, kidney damage, damage to blood vasculature, **hypertension**, retinopathy, damage to lens proteins, cataracts, peripheral neuropathy, or osteoarthritis. Thus, 3-(2-phenyl-2-hydroxyethyl)-4,5-dimethylthiazolium chloride (I)was prepared by the reduction of 2-chloroacetophenone followed by the reaction of the resulting alc. with 4,5-dimethylthiazole. Tablets contained I 50, starch 50, mannitol 75, mg stearate 2, and stearic acid 2 mg/tablet.
2001:635892 Document Number 135:200476 Thiazolium compounds and treatments of disorders associated with skin aging. Wagle, Dilip; Vasan, Sarah; Egan, Jack (Alteon, Inc., USA). PCT Int. Appl. WO 2001062250 A1 20010830, 32 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US5868 20010223. PRIORITY: US 2000-PV184266 20000223.
AB . . . skin, treating disorders such as diabetes or treating or preventing adverse sequelae of diabetes, kidney damage, damage to blood vasculature, **hypertension**, retinopathy, damage to lens proteins, cataracts, peripheral neuropathy, or osteoarthritis. Thus, 3-(2-phenyl-2-hydroxyethyl)-4,5-dimethylthiazolium chloride (I)was prepared by the reduction of 2-chloroacetophenone. . .
IT Antiarthritics
Antidiabetic agents
Antihypertensives
Blood vessel, disease
Dentifrices
Mouthwashes
Skin, disease
(thiazolium compds. for treatments of disorders associated with skin

aging)

IT **356759-42-7P 356759-43-8P 356759-44-9P**
356759-45-0P 356759-46-1P 356759-47-2P
356759-48-3P **356759-50-7P 356759-52-9P**
356759-53-0P 356759-54-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(thiazolium compds. for treatments of disorders associated with skin aging)

IT **356759-42-7P 356759-43-8P 356759-44-9P**
356759-45-0P 356759-46-1P 356759-47-2P
356759-50-7P 356759-52-9P 356759-53-0P
356759-54-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(thiazolium compds. for treatments of disorders associated with skin aging)

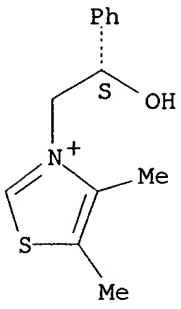
RN 356759-42-7 HCAPLUS
CN Thiazolium, 3-(2-hydroxy-2-phenylethyl)-4,5-dimethyl-, chloride (9CI) (CA INDEX NAME)



● Cl^-

RN 356759-43-8 HCAPLUS
CN Thiazolium, 3-[(2S)-2-hydroxy-2-phenylethyl]-4,5-dimethyl-, chloride (9CI) (CA INDEX NAME)

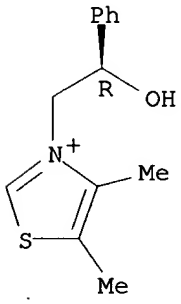
Absolute stereochemistry. Rotation (-).



● Cl^-

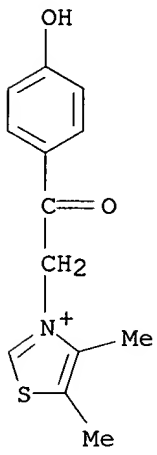
RN 356759-44-9 HCAPLUS
CN Thiazolium, 3-[(2R)-2-hydroxy-2-phenylethyl]-4,5-dimethyl-, chloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



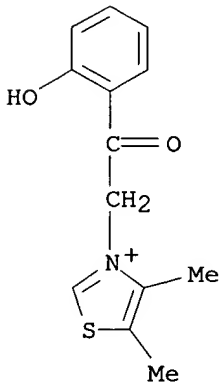
● Cl^-

RN 356759-45-0 HCAPLUS
CN Thiazolium, 3-[2-(4-hydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



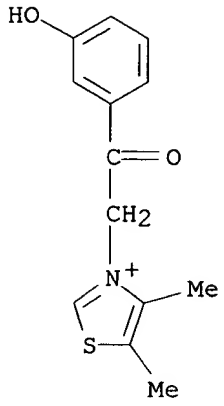
● Br^-

RN 356759-46-1 HCAPLUS
CN Thiazolium, 3-[2-(2-hydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



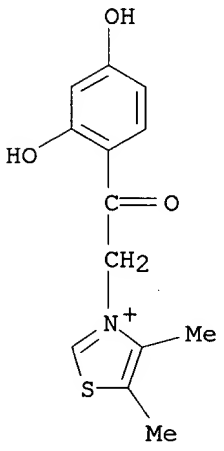
● Br^-

RN 356759-47-2 HCAPLUS
CN Thiazolium, 3-[2-(3-hydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



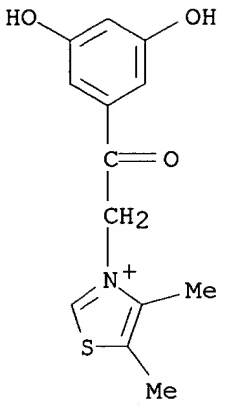
● Br^-

RN 356759-50-7 HCAPLUS
CN Thiazolium, 3-[2-(2,4-dihydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



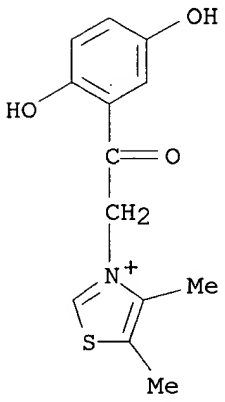
● Br^-

RN 356759-52-9 HCAPLUS
CN Thiazolium, 3-[2-(3,5-dihydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



● Br^-

RN 356759-53-0 HCAPLUS
CN Thiazolium, 3-[2-(2,5-dihydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



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RN 356759-54-1 HCAPLUS
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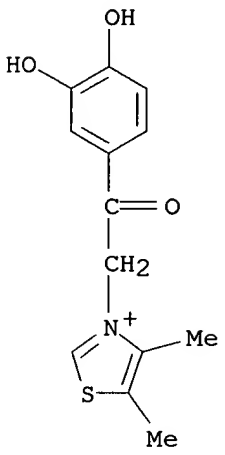


● Br^-

L6 ANSWER 11 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN

AB A review with 6 refs. Vascular and/or myocardial stiffness is a major problem in ageing, diabetes, **hypertension** and heart failure. The development of the stiffness is partly due to the formation of glucose-dependent cross-links in the collagen. ALT-711 cleaves these cross-links. In aged-rhesus monkeys, ALT-711 decreases vascular stiffness and this effect is reversible. ALT-711 also decreases myocardial stiffness in the monkeys but this effect is not reversible in 39 wk. ALT-711 has potential in the treatment of the stiffness associated with diabetes, **hypertension** and heart failure.

2001:321927 Document Number 135:131603 ALT-711 decreases cardiovascular stiffness and has potential in diabetes, **hypertension** and heart failure. Doggrell, Sheila A. (Doggrell Biomedical Communications, Auckland, N. Z.). Expert Opinion on Investigational Drugs, 10(5), 981-983 (English) 2001. CODEN: EOIDER. ISSN: 1354-3784. Publisher: Ashley Publications Ltd..

TI ALT-711 decreases cardiovascular stiffness and has potential in diabetes, **hypertension** and heart failure

AB A review with 6 refs. Vascular and/or myocardial stiffness is a major problem in ageing, diabetes, **hypertension** and heart failure. The development of the stiffness is partly due to the formation of glucose-dependent cross-links in the collagen.. . . this effect is not reversible in 39 wk. ALT-711 has potential in the treatment of the stiffness associated with diabetes, **hypertension** and heart failure.

ST review cardiovascular stiffness ALT711 diabetes **hypertension**; heart failure arterial stiffness ALT711 review

IT Aging, animal
Diabetes mellitus
Hypertension
(ALT-711 decreases cardiovascular stiffness and has potential in diabetes, **hypertension** and heart failure)

IT Heart, disease
(failure; ALT-711 decreases cardiovascular stiffness and has potential in diabetes, **hypertension** and heart failure)

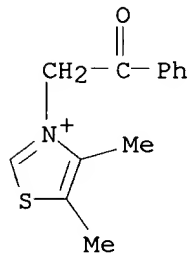
IT Artery, disease
(stiffness; ALT-711 decreases cardiovascular stiffness and has potential in diabetes, **hypertension** and heart failure)

IT **341028-37-3**, ALT 711
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALT-711 decreases cardiovascular stiffness and has potential in diabetes, **hypertension** and heart failure)

IT **341028-37-3**, ALT 711
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALT-711 decreases cardiovascular stiffness and has potential in diabetes, **hypertension** and heart failure)

RN 341028-37-3 HCAPLUS

CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)-, chloride (9CI) (CA INDEX NAME)



● Cl^-

L6 ANSWER 12 OF 18 HCAPLUS COPYRIGHT 2005 ACS on STN

AB Nonenzymic glycosylation and crosslinking of proteins by glucose contributes to an age-associated increase in vascular and myocardial stiffness. Some recently synthesized thiazolium compds. selectively break these protein cross-links, reducing collagen stiffness. We investigated the effects of 3-phenacyl-4,5-dimethylthiazolium chloride (ALT-711) on arterial and left ventricular (LV) properties and their coupling in old, healthy, nondiabetic Macaca mulatta primates (age 21±3.6 yr). Serial measurements of arterial stiffness indexes [i.e., aortic pulse wave velocity (PWV) and augmentation (AGI) of carotid arterial pressure waveform] as well as echocardiog. detns. of LV structure and function were made before and for 39 wk after 11 i.m. injections of ALT-711 at 1.0 mg/kg body weight every other day. Heart rate, brachial **blood pressure**, and body weight were unchanged by the drug. PWV and AGI decreased to a nadir at 6 wk [PWV to 74.2±4.4% of baseline (B), P = 0.007; AGI to 41±7.3% of B, P = 0.046], and thereafter gradually returned to baseline. Concomitant increases in LV end **diastolic** diameter to 116.7±2.7% of B, P = 0.02; stroke volume index (SVindex) to 173.1±40.1% of B, P = 0.01; and **systolic** fractional shortening to 180±29.7% of B, P = 0.01 occurred after drug treatment The LV end **systolic** pressure/SVindex, an estimate of total LV

vascular load, decreased to 60±12.1% of B (P = 0.02). The LV end **systolic** diameter/SVindex, an estimate of arterio-ventricular coupling, was improved (decreased to 54.3±11% of B, P < 0.002). Thus, in healthy older primates without diabetes, ALT-711 improved both arterial and ventricular function and optimized ventriculo-vascular coupling. This previously unidentified cross-link breaker may be an effective pharmacol. therapy to improve impaired cardiovascular function that occurs in the context of heart failure associated with aging, diabetes, or **hypertension**, conditions in which arterial and ventricular stiffness are increased.

2001:120548 Document Number 134:290192 A cross-link breaker has sustained effects on arterial and ventricular properties in older rhesus monkeys. Vaitkevicius, Peter V.; Lane, Mark; Spurgeon, Harold; Ingram, Donald K.; Roth, George S.; Egan, John J.; Vasan, Sara; Wagle, Dilip R.; Ulrich, Peter; Brines, Michael; Wuerth, Jean Paul; Cerami, Anthony; Lakatta, Edward G. (Intramural Research Program, Gerontology Research Center, National Institute on Aging, National Institutes of Health, Baltimore, MD, 21224, USA). Proceedings of the National Academy of Sciences of the United States of America, 98(3), 1171-1175 (English) 2001. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.

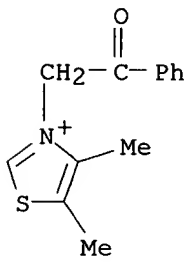
AB . . . for 39 wk after 11 i.m. injections of ALT-711 at 1.0 mg/kg body weight every other day. Heart rate, brachial **blood pressure**, and body weight were unchanged by the drug. PWV and AGI decreased to a nadir at 6 wk [PWV to. . . 0.007; AGI to 41±7.3% of B, P = 0.046], and thereafter gradually returned to baseline. Concomitant increases in LV end **diastolic** diameter to 116.7±2.7% of B, P = 0.02; stroke volume index (SVindex) to 173.1±40.1% of B, P = 0.01; and **systolic** fractional shortening to 180±29.7% of B, P = 0.01 occurred after drug treatment The LV end **systolic** pressure/SVindex, an estimate of total LV vascular load, decreased to 60±12.1% of B (P = 0.02). The LV end **systolic** diameter/SVindex, an estimate of arterio-ventricular coupling, was improved (decreased to 54.3±11% of B, P < 0.002). Thus, in healthy older. . . pharmacol. therapy to improve impaired cardiovascular function that occurs in the context of heart failure associated with aging, diabetes, or **hypertension**, conditions in which arterial and ventricular stiffness are increased.

IT **181069-80-7**, ALT-711
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of cross-link breaker on arterial and ventricular properties in aging rhesus monkeys)

IT **181069-80-7**, ALT-711
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of cross-link breaker on arterial and ventricular properties in aging rhesus monkeys)

RN 181069-80-7 HCAPLUS

CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)-, bromide (9CI) (CA INDEX NAME)



● Br^-

L6 ANSWER 13 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

AB Advanced glycation end product (AGE) formation that occurs with aging and diabetes leads to the cross-linking of proteins and subsequent changes in the physicochemical properties of tissues. Cellular responses to AGE that lead to either pathological conditions or removal of AGE are mediated by a number of receptors that have been identified on various cell types such as macrophages, endothelial cells, and smooth-muscle cells. Mechanisms by which AGE affect the cardiovascular system include AGE cross-linking of long-lived proteins such as collagen and elastin and altered cellular responses. Alagebrium (3-plenacyl-4,5-dimethylthiazolium chloride, ALT-711) is the first drug in a new class of thiazolium therapeutic agents that break established AGE cross-links between proteins. In animal studies, alagebrium was effective in reducing large artery stiffness, slowing pulsewave velocity, enhancing cardiac output, and improving left ventricular **diastolic** distensibility. In human studies to determine safety and efficacy, alagebrium was safe and well tolerated. In the first phase 2 clinical study, alagebrium improved arterial compliance in elderly patients with vascular stiffening. In two subsequent phase 2 clinical studies, one addressing **diastolic** heart failure, and the other addressing **systolic hypertension**, alagebrium was effective, in improving cardiac function and uncontrolled sysiolic **blood pressure**, particularly in more severely affected patients. Additional clinical studies to determine the utility of alagebrium in creating cardiovascular disorders associated with aging are in progress. Copyright 2004 American Journal of **Hypertension**, Ltd.

2005:91053 Document Number: PREV200500090913. Advanced glycation end-product cross-link breakers - A novel approach to cardiovascular pathologies related to the aging process. Bakris, George L. [Reprint Author]; Bank, Alan J.; Kass, David A.; Neutel, Joel M.; Preston, Richard A.; Oparil, Suzanne. Med CtrDept Prevent Med, Rush Univ, 1700 W Van Buren,Suite 470, Chicago, IL, 60612, USA. George-Bakris@rush.edu. American Journal of Hypertension, (December 2004) Volume 17, Number 12, Suppl. S, Part 2, pp. 23S-30S. print.
CODEN: AJHYE6. ISSN: 0895-7061. Language: English.

AB. . . animal studies, alagebrium was effective in reducing large artery stiffness, slowing pulsewave velocity, enhancing cardiac output, and improving left ventricular **diastolic** distensibility. In human studies to determine safety and efficacy, alagebrium was safe and well tolerated. In the first phase 2. . . study, alagebrium improved

arterial compliance in elderly patients with vascular stiffening. In two subsequent phase 2 clinical studies, one addressing **diastolic** heart failure, and the other addressing **systolic hypertension**, alagebrium was effective, in improving cardiac function and uncontrolled sysiolic **blood pressure**, particularly in more severely affected patients. Additional clinical studies to determine the utility of alagebrium in creating cardiovascular disorders associated with aging are in progress. Copyright 2004 American Journal of **Hypertension**, Ltd.

IT . . .
(Human Medicine, Medical Sciences); Pharmacology
IT Parts, Structures, & Systems of Organisms
artery: circulatory system; heart: circulatory system
IT Diseases
diastolic heart failure: heart disease, drug therapy
Heart Failure, Congestive (MeSH)
IT Diseases
left ventricular **diastolic** distensibility: heart disease, drug therapy
IT Diseases
systolic hypertension: vascular disease, drug therapy
Hypertension (MeSH)
IT Diseases
vascular stiffening: vascular disease, drug therapy, epidemiology
IT Chemicals & Biochemicals
advanced glycation end-products; alagebrium [ALT-711]: **antihypertensive**-drug, cardiotonic-drug, cardiovascular-drug, cross-link breaker, efficacy, preclinical trial, safety, tolerance, clinical trial; collagen; elastin
IT Miscellaneous Descriptors
aging; cardiac function; cellular response; **systolic blood pressure**
RN **181069-80-7Q** (alagebrium)
341028-37-3Q (alagebrium)
181069-80-7Q (ALT-711)
341028-37-3Q (ALT-711)

L6 ANSWER 14 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
2004:401174 Document No.: PREV200400397666. Crosslink breakers: a new approach to cardiovascular therapy. Susic, Dinko [Reprint Author]; Varagic, Jasmina; Ahn, Jwari; Frohlich, Edward D.. Div ResHypertens Res Lab, Ochsner Clin Fdn, 1520 Jefferson Highway, New Orleans, LA, 70121, USA. Current Opinion in Cardiology, (July 2004) Vol. 19, No. 4, pp. 336-340. print.
ISSN: 0268-4705 (ISSN print). Language: English.
IT . . .
disorders: vascular disease, drug therapy, mortality, therapy
Cardiovascular Diseases (MeSH)
IT Diseases
diabetes: endocrine disease/pancreas, metabolic disease
Diabetes Mellitus (MeSH)
IT Diseases
hypertension: vascular disease
Hypertension (MeSH)
IT Diseases

renal disorders: urologic disease, drug therapy, therapy
IT Chemicals & Biochemicals
ALT-711: antidiabetic-drug, **antihypertensive**-drug, cardiovascular-drug, renal-acting-drug; advanced glycation end-products; collagen; glucose
RN **181069-80-7Q** (ALT-711)
341028-37-3Q (ALT-711)
50-99-7Q (glucose)
58367-01-4Q (glucose)

L6 ANSWER 15 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
2004:378805 Document No.: PREV200400377419. Breaker of glycated collagen cross-links, ALT-711, improves left ventricular function and aortic distensibility in elderly spontaneously **hypertensive** rats.
Susic, Dinko [Reprint Author]; Varagic, Jasmina; Ahn, Jwari; Matavelli, Louis C; Frohlich, Edward D.. Div Res, Alton Ochsner Med Fdn and Ochsner Clin, New Orleans, LA, 70121, USA. American Journal of Hypertension, (May 2004) Vol. 17, No. 5, Part 2, pp. 169A. print.
Meeting Info.: 19th Annual Scientific Meeting of the American Society of Hypertension. New York, NY, USA. May 18-22, 2004. American Society of Hypertension.
CODEN: AJHYE6. ISSN: 0895-7061. Language: English.
TI Breaker of glycated collagen cross-links, ALT-711, improves left ventricular function and aortic distensibility in elderly spontaneously **hypertensive** rats.
IT . . .
diameter, distensibility, stiffness; carotid artery: circulatory system, right; femoral artery: circulatory system; heart ventricle: circulatory system, function, left
IT Diseases
hypertension: vascular disease, pathology
Hypertension (MeSH)
IT Diseases
left ventricular dysfunction: heart disease, epidemiology, etiology, pathology
Ventricular Dysfunction, Left (MeSH)
IT Chemicals & Biochemicals
ALT-711: collagen. . .
IT Miscellaneous Descriptors
aging; cardiac output; **diastolic** pressure; heart rate; mean arterial pressure; pulse pressure; pulse wave velocity; total peripheral resistance
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
spontaneously **hypertensive** rat (common): immature, mature, animal model, male
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
RN **181069-80-7Q** (ALT-711)
341028-37-3Q (ALT-711)

L6 ANSWER 16 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on

STN
2004:378696 Document No.: PREV200400377310. A clinical trial of an age cross-link breaker, ALT-711, in **systolic hypertension**.
Bakris, G. L. [Reprint Author]; Bank, A.; Kass, D. A.; Neutel, J.; Preston, R.. Med Ctr, Rush Univ, Chicago, IL, 60612, USA. American Journal of Hypertension, (May 2004) Vol. 17, No. 5, Part 2, pp. 127A-128A. print.
Meeting Info.: 19th Annual Scientific Meeting of the American Society of Hypertension. New York, NY, USA. May 18-22, 2004. American Society of Hypertension.
CODEN: AJHYE6. ISSN: 0895-7061. Language: English.
TI A clinical trial of an age cross-link breaker, ALT-711, in **systolic hypertension**.
IT . . .
Medicine, Medical Sciences); Pharmacology
IT Parts, Structures, & Systems of Organisms
artery: circulatory system, pulse pressure; blood: blood and lymphatics, **diastolic** pressure, **systolic** pressure
IT Diseases
systolic hypertension: vascular disease, drug therapy, prevention and control
Hypertension (MeSH)
IT Chemicals & Biochemicals
ALT-711: **antihypertensive**-drug, cardiovascular-drug, dosage, efficacy, novel advanced glycation end product cross-link breaker, safety, tolerability, clinical trial; advanced glycation end product: cross-link; **antihypertension** drug: **antihypertensive** -drug, cardiovascular-drug
IT Methods & Equipment
ambulatory **blood pressure** monitoring: clinical techniques, diagnostic techniques
IT Miscellaneous Descriptors
arterial compliance
RN **181069-80-7Q** (ALT-711)
341028-37-3Q (ALT-711)

L6 ANSWER 17 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
2004:35536 Document No.: PREV200400033330. Effect of ALT-711, a novel glucose cross-link breaker, in the treatment of **diastolic** heart failure.
Kitzman, D. W. [Reprint Author]; Zile, M. R.; Little, W. C. [Reprint Author]; Hundley, W. G. [Reprint Author]; O'Brien, T. X.; DeGroof, R. C.. IM/Cardiology, Wake Forest University Health Sciences, Winston-Salem, NC, USA. European Heart Journal, (August-September 2003) Vol. 24, No. Abstract Supplement, pp. 408. print.
Meeting Info.: Congress of the European Society of Cardiology. Vienna, Austria. August 30-September 03, 2003. European Society of Cardiology.
ISSN: 0195-668X (ISSN print). Language: English.
TI Effect of ALT-711, a novel glucose cross-link breaker, in the treatment of **diastolic** heart failure.
IT . . .
& Systems of Organisms
LV: circulatory system, mass, volume, left ventricle; aorta: circulatory system, distensibility; heart: circulatory system
IT Diseases
diastolic heart failure: heart disease
Heart Failure, Congestive (MeSH)
IT Chemicals & Biochemicals

ACE inhibitor [angiotensin converting enzyme inhibitor]: angiotensin-converting enzyme inhibitor-drug,. . .

IT Methods & Equipment
magnetic resonance imaging: clinical techniques, diagnostic techniques, imaging and microscopy techniques, laboratory techniques

IT Miscellaneous Descriptors
LV **diastolic** filling [left ventricular **diastolic** filling]; **blood pressure**; early **diastolic** flow velocity; early **diastolic** mitral annulus velocity; peak exercise oxygen consumption; quality of life

RN **181069-80-7Q** (ALT-711)
341028-37-3Q (ALT-711)

L6 ANSWER 18 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

2001:184349 Document No.: PREV200100184349. Cardiovascular effects of an advanced glycation end product breaker ALT-711 in adult spontaneously **hypertensive** rats. Varagic, Jasmina [Reprint author]; Susic, Dinko [Reprint author]; Frohlich, Edward D. [Reprint author]. Alton Ochsner Medical Foundation, New Orleans, LA, USA. Journal of the American College of Cardiology, (February, 2001) Vol. 37, No. 2 Supplement A, pp. 290A-291A. print.
Meeting Info.: 50th Annual Scientific Session of the American College of Cardiology. Orlando, Florida, USA. March 18-21, 2001. American College of Cardiology.
CODEN: JACCDI. ISSN: 0735-1097. Language: English.

TI Cardiovascular effects of an advanced glycation end product breaker ALT-711 in adult spontaneously **hypertensive** rats.

IT . . .

Miscellaneous Descriptors
coronary flow reserve; coronary hemodynamics; left ventricular coronary blood flow; left ventricular function; mean arterial pressure; minimal coronary **vascular resistance**; systemic hemodynamics; total peripheral resistance; Meeting Abstract

ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
spontaneously **hypertensive** rat: adult, animal model, male
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN **181069-80-7Q** (ALT-711)
341028-37-3Q (ALT-711)

FILE 'MEDLINE' ENTERED AT 16:45:53 ON 04 AUG 2005

FILE 'HCAPLUS' ENTERED AT 16:45:53 ON 04 AUG 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE 'BIOSIS' ENTERED AT 16:45:53 ON 04 AUG 2005

FILE 'EMBASE' ENTERED AT 16:45:53 ON 04 AUG 2005

=> d his

(FILE 'HOME' ENTERED AT 16:27:23 ON 04 AUG 2005)

FILE 'REGISTRY' ENTERED AT 16:27:31 ON 04 AUG 2005
L1 STRUCTURE UPLOADED
L2 1 S L1 SSS SAM
L3 47 S L1 SSS FULL

FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE' ENTERED AT 16:34:33 ON 04 AUG 2005
L4 71 S L3
L5 63 DUP REM L4 (8 DUPLICATES REMOVED)
L6 18 S L5 AND (SYSTOL? OR HYPERTENS? OR DIASTOL? OR BLOOD(2A)PRESSUR
L7 0 S L6 AND HYDROCHLOROTHIAZ?

FILE 'REGISTRY' ENTERED AT 16:41:54 ON 04 AUG 2005
E HYDROCHLOROTHIAZIDE/CN
L8 1 S E3

FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE' ENTERED AT 16:42:33 ON 04 AUG 2005
L9 25687 S L8
L10 0 S L6 AND L9

FILE 'STNGUIDE' ENTERED AT 16:43:52 ON 04 AUG 2005

FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE' ENTERED AT 16:45:53 ON 04 AUG 2005

=> s l4 and l9
L11 2 L4 AND L9

=> d l11 abs cbib kwic hitstr 1-2

L11 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the composition to the patient. The peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prepared from Glu(OBut)NCA and cephalexin hydrochloride.
2002:556104 Document Number 137:109489 Compositions comprising a polypeptide and an active agent. Piccariello, Thomas; Olon, Lawrence P.; Kirk, Randal J. (USA). U.S. Pat. Appl. Publ. US 2002099013 A1 20020725, 34 pp.

Delacroix

(English). CODEN: USXXCO. APPLICATION: US 2001-933708 20010822. PRIORITY: US 2000-PV247928; 20001114; US 2000-PV247621; 20001114; US 2000-PV247620; 20001114; US 2000-PV247595; 20001114; US 2000-PV247594; 20001114; US 2000-PV247635; 20001114; US 2000-PV247634; 20001114; US 2000-PV247606; 20001114; US 2000-PV247607; 20001114; US 2000-PV247608; 20001114; US 2000-PV247609; 20001114; US 2000-PV247610; 20001114; US 2000-PV247611; 20001114; US 2000-PV247702; 20001114; US 2000-PV247701; 20001114; US 2000-PV247700; 20001114; US 2000-PV247699; 20001114; US 2000-PV247698; 20001114; US 2000-PV247807; 20001114; US 2000-PV247833; 20001114.

IT 50-06-6, Phenobarbital, biological studies 50-18-0, Cyclophosphamide 50-35-1, Thalidomide 50-44-2, Mercaptopurine 50-78-2, Acetylsalicylic acid 50-81-7, Vitamin C, biological studies 51-21-8, Fluorouracil 51-61-6, Dopamine, biological studies 51-63-8, Dextroamphetamine sulfate 51-98-9, Norethindrone acetate 52-01-7, Spironolactone 52-24-4, Thiotepa 52-86-8, Haloperidol 53-36-1, Methylprednisolone Acetate 54-31-9, Furosemide 55-63-0, Nitroglycerin 57-63-6, Ethinyl estradiol 58-08-2, Caffeine, biological studies 58-18-4, Methyltestosterone 58-25-3, Chlordiazepoxide 58-33-3, Promethazine hydrochloride 58-55-9, Theophylline, biological studies 58-61-7, Adenosine, biological studies **58-93-5**, Hydrochlorothiazide 59-42-7, Phenylephrine 60-54-8, Tetracycline 60-87-7, Promethazine 64-31-3, Morphine Sulfate 67-20-9, Nitrofurantoin 67-92-5, Dicyclomine hydrochloride 68-19-9, Vitamin B12 68-22-4, Norethindrone 71-58-9, Medroxyprogesterone acetate 71-68-1, Hydromorphone hydrochloride 74-79-3, Arginine, biological studies 76-41-5, Oxymorphone 76-42-6, Oxycodone 76-58-4, Ethylmorphine 78-44-4, Carisoprodol 84-02-6, Prochlorperazine maleate 87-08-1, Penicillin V 87-33-2, Isosorbide Dinitrate 89-57-6, Mesalamine 90-82-4, Pseudoephedrine 93-14-1, Guaifenesin 113-45-1, Methylphenidate 113-52-0 113-92-8, Chlorpheniramine maleate 114-07-8, Erythromycin 124-90-3, Oxycodone hydrochloride 125-28-0, Dihydrocodeine 125-29-1, Hydrocodone 125-33-7, Primidone 125-71-3, Dextromethorphan 128-13-2, Ursodiol 129-06-6, Warfarin Sodium 132-17-2, Benzatropine methanesulfonate 143-52-2, Methyldihydromorphinone 143-71-5, Hydrocodone bitartrate 152-11-4, Verapamil hydrochloride 297-76-7, Ethynodiol diacetate 298-46-4, Carbamazepine 298-59-9, Methylphenidate hydrochloride 303-49-1, Clomipramine 315-30-0, Allopurinol 318-98-9, Propranolol Hydrochloride 378-44-9, Betamethasone 379-79-3, Ergotamine Tartrate 437-38-7, Fentanyl 439-14-5, Diazepam 446-86-6, Azathioprine 466-99-9, Hydromorphone 469-62-5, Propoxyphene 509-60-4, Dihydromorphine 514-36-3, Fludrocortisone acetate 541-15-1, Levocarnitine 549-18-8, Amitriptyline hydrochloride 554-13-2, Lithium Carbonate 561-27-3, Diacetylmorphine 595-33-5, Megestrol acetate 604-75-1, Oxazepam 630-93-3, Sodium phenytoin 657-24-9, Metformin 745-65-3, Alprostadil 747-36-4, Hydroxychloroquine sulfate 797-63-7, Levonorgestrel 846-49-1, Lorazepam 846-50-4, Temazepam 894-71-3, Nortriptyline hydrochloride 959-24-0, Sotalol hydrochloride 1134-47-0, Baclofen 1403-66-3, Gentamicin 1404-93-9, Vancomycin hydrochloride 1501-84-4, Rimantadine hydrochloride 1508-65-2, Oxybutynin chloride 1622-61-3, Clonazepam 1665-48-1, Metaxalone 1744-22-5, Riluzole 1951-25-3, Amiodarone 2078-54-8, Propofol 2152-34-3, Pemoline 2375-03-3, Methylprednisolone sodium succinate 4205-91-8 4682-36-4, Orphenadrine citrate 4759-48-2, Isotretinoin 5786-21-0, Clozapine 6202-23-9, Cyclobenzaprine hydrochloride 6493-05-6, Pentoxifylline 6533-00-2, Norgestrel 7280-37-7, Estropipate 7414-83-7, Etidronate disodium 9002-60-2, Adrenocorticotrophic hormone, biological studies 9002-69-1,

Relaxin 9005-49-6, Heparin, biological studies 9014-42-0, Thrombopoietin 9039-53-6, Urokinase 9041-08-1, Dalteparin sodium 9041-92-3, .α.1-Protease inhibitor 9080-79-9, Sodium polystyrene sulfonate 10238-21-8, Glyburide 11005-12-2, β-Phytosterol 11056-06-7, Bleomycin 11140-85-5, Glucagon hydrochloride 13311-84-7, Flutamide 13614-98-7, Minocycline hydrochloride 14124-50-6, Hydrochlorothiazide-triamterene mixture 14611-52-0, Selegiline hydrochloride 14838-15-4, Phenylpropanolamine 15307-79-6, Diclofenac sodium 15663-27-1, Cisplatin 15686-71-2, Cephalexin 17140-78-2, Propoxyphene napsylate 17560-51-9, Metolazone 18559-94-9, Albuterol 19767-45-4, Mesna 20537-88-6, Amifostine 20830-75-5, Digoxin 21062-37-3D, analogs 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 22071-15-4, Ketoprofen 23031-32-5, Terbutaline sulfate 25316-40-9, Doxorubicin hydrochloride 25322-68-3, Polyethylene glycol 25332-39-2, Trazodone hydrochloride 25614-03-3, Bromocriptine 26159-34-2, Naproxen sodium 26787-78-0, Amoxicillin 27164-46-1, Cefazolin sodium 27314-97-2, Tirapazamine 28860-95-9, Carbidopa 28981-97-7, Alprazolam 29094-61-9, Glipizide 29354-16-3, Thyronine, iodo- 31677-93-7, Bupropion hydrochloride 32222-06-3, Calcitriol 32780-64-6, Labetalol hydrochloride 33069-62-4, Paclitaxel 33286-22-5, Diltiazem hydrochloride 33419-42-0, Etoposide 33564-30-6, Cefoxitin sodium 34552-83-5, Loperamide hydrochloride 34580-13-7, Ketotifen 35189-28-7, Norgestimate 36282-47-0, Tramadol hydrochloride 36505-84-7, Buspirone 36791-04-5, Ribavirin 37296-80-3, Colestipol hydrochloride 38398-32-2, Ganaxolone 41340-25-4, Etodolac 41575-94-4, Carboplatin 42200-33-9, Nadolol 42617-41-4, Activated protein C 42924-53-8, Nabumetone 49562-28-9, Fenofibrate 49842-07-1, Tobramycin sulfate 50370-12-2, Cefadroxil 50700-72-6, Vecuronium bromide 51321-79-0, Sparfosic acid 51481-61-9, Cimetidine 51773-92-3, Mefloquine hydrochloride 52232-67-4, Teriparatide 53885-35-1, Ticlopidine hydrochloride 53994-73-3, Cefaclor 54024-22-5, Desogestrel 54143-56-5, Flecainide acetate 54182-58-0, Sucralfate 54910-89-3, Fluoxetine 54965-24-1, Tamoxifen citrate 55079-83-9, Acitretin 56180-94-0, Acarbose 56238-63-2, Cefuroxime sodium 57109-90-7, Clorazepate dipotassium 57248-88-1, Pamidronate disodium 57852-57-0, Idarubicin hydrochloride 58579-51-4, Anagrelide hydrochloride 58786-99-5, Butorphanol tartrate 59122-46-2, Misoprostol 59703-84-3, Piperacillin sodium 59729-32-7, Citalopram hydrobromide 59865-13-3, Cyclosporin 59989-18-3, Eniluracil 60142-96-3, Gabapentin 60205-81-4, Ipratropium 60748-06-3, Gastrin 17 61718-82-9, Fluvoxamine maleate 62288-83-9, Desmopressin acetate 62571-86-2, Captopril 63074-08-8, Terazosin hydrochloride 63675-72-9, Nisoldipine 64221-86-9, Imipenem 64461-82-1, Tizanidine hydrochloride 64485-93-4, Cefotaxime sodium 64544-07-6, Cefuroxime axetil 65277-42-1, Ketoconazole 65646-68-6, Fenretinide 65807-02-5, Goserelin 66085-59-4, Nimodipine 66104-22-1, Pergolide 66357-35-5, Ranitidine 66722-44-9, Bisoprolol 67889-72-9, Acetaminophen-codeine phosphate mixture 67992-58-9, Sodium ioxaglate 68562-41-4, Mecasermin 68693-11-8, Modafinil 68844-77-9, Astemizole 69655-05-6, Didanosine 70458-96-7, Norfloxacin 70476-82-3, Mitoxantrone hydrochloride 72509-76-3, Felodipine 72558-82-8, Ceftazidime 72956-09-3, Carvedilol 73334-07-3, Iopromide 73573-87-2, Formoterol 73590-58-6, Omeprazole 74103-06-3, Ketorolac 74191-85-8, Doxazosin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising a polypeptide and an active agent)

IT 74356-00-6, Cefotetan disodium 74381-53-6, Leuprolide acetate 74469-00-4, Amoxicillin-potassium clavulanate mixture 75330-75-5, Lovastatin 75695-93-1, Isradipine 75706-12-6, Leflunomide

75847-73-3, Enalapril 75970-99-9, Norastemizole 76470-66-1, Loracarbef 76547-98-3, Lisinopril 76584-70-8, Divalproex sodium 76820-74-1, Sodium meglumine ioxaglate 76824-35-6, Famotidine 76963-41-2, Nizatidine 78246-49-8, Paroxetine hydrochloride 78628-80-5, Terbinafine hydrochloride 78755-81-4, Flumazenil 79307-93-0, Azelastine hydrochloride 79350-37-1, Cefixime 79517-01-4, Octreotide acetate 79794-75-5, Loratadine 79902-63-9, Simvastatin 81098-60-4, Cisapride 81103-11-9, Clarithromycin 81129-83-1, Cilastatin sodium 81131-70-6, Pravastatin sodium 81409-90-7, Cabergoline 81627-83-0, M-CSF 82410-32-0, Ganciclovir 82419-36-1, Ofloxacin 82586-52-5, Moexipril hydrochloride 82586-55-8, Quinapril hydrochloride 82626-48-0, Zolpidem 82640-04-8, Raloxifene hydrochloride 82657-92-9, Prourokinase 82752-99-6, Nefazodone hydrochloride 83015-26-3, Tomoxetine 83881-52-1, Cetirizine hydrochloride 83905-01-5, Azithromycin 83928-66-9, Gepirone hydrochloride 84057-84-1, Lamotrigine 84485-00-7, Sibutramine hydrochloride 84625-61-6, Itraconazole 85650-52-8, Mirtazapine 85721-33-1, Ciprofloxacin 86050-77-3, Gadopentetate dimeglumine 86386-73-4, Fluconazole 86541-74-4, Benazepril hydrochloride 87239-81-4, Cefpodoxime proxetil 87333-19-5, Ramipril 87679-37-6, Trandolapril 90357-06-5, Bicalutamide 90566-53-3, Fluticasone 91374-20-8, Ropinirole hydrochloride 91421-42-0, Rubitecan 91832-40-5, Cefdinir 92134-98-0, Fosphenytoin sodium 92339-11-2, Iodixanol 92665-29-7, Cefprozil 93379-54-5, Esatenolol 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 95233-18-4, Atovaquone 95635-56-6, Ranolazine hydrochloride 95896-08-5, Anaritide 96036-03-2, Meropenem 96829-58-2, Orlistat 96946-42-8, Cisatracurium besylate 97240-79-4, Topiramate 97322-87-7, Troglitazone 97519-39-6, Ceftibuten 98048-97-6, Fosinopril 98319-26-7, Finasteride 98418-47-4, Metoprolol succinate 99300-78-4, Venlafaxine hydrochloride 99614-01-4, Ondansetron hydrochloride 100286-90-6, Irinotecan hydrochloride 100286-97-3, Milrinone lactate 100986-85-4, Levofloxacin 103475-41-8, Tepoxalin 103577-45-3, Lansoprazole 104227-87-4, Famciclovir 104632-25-9, Pramipexole dihydrochloride 106266-06-2, Risperidone 106392-12-5, Poloxamer 188 106861-44-3, Mivacurium chloride 107007-99-8, Granisetron hydrochloride 107753-78-6, Zafirlukast 111470-99-6, Amlodipine besylate 111974-72-2, Quetiapine fumarate 112108-01-7, Ecopipam 112529-15-4, Pioglitazone hydrochloride 112573-73-6, Ecadotril 112733-06-9, Zenarestat 113427-24-0, Epoetin alfa 114977-28-5, Docetaxel 115956-13-3, Dolasetron mesylate 116539-59-4, Duloxetine 117976-90-6, Rabeprazole sodium 118390-30-0, Interferon alfacon-1 119302-91-9, Rocuronium bromide 119413-54-6, Topotecan hydrochloride 120011-70-3, Donepezil hydrochloride 120066-54-8, Gadoteridol 120202-66-6, Clopidogrel bisulfate 120511-73-1, Anastrozole 120635-74-7, Cilansetron 121032-29-9, Nelarabine 121181-53-1D, PEGylated 121584-18-7, Valspodar 122111-03-9, Gemcitabine hydrochloride 123122-55-4, Candoxatril 123258-84-4, Itasetron 124584-08-3, Nesiritide 124750-99-8, Losartan potassium 124832-27-5, Valacyclovir hydrochloride 124937-52-6, Tolterodine tartrate 125317-39-7, Vinorelbine tartrate 126544-47-6, Ciclesonide 127254-12-0, Sitafloxacin 127779-20-8, Saquinavir 128298-28-2, Remacemide 128794-94-5, Mycophenolate mofetil 129318-43-0, Alendronate sodium 129580-63-8, Satraplatin 129618-40-2, Nevirapine 129722-12-9, Aripiprazole 130018-77-8, Levocetirizine 130325-35-8, PD 135158 131918-61-1, Paricalcitol 132449-46-8, Lesopitron 132539-06-1, Olanzapine 133107-64-9, Insulin lispro 133737-32-3, Pagoclone 134523-03-8, Atorvastatin calcium 134564-82-2, Befloxatone 134678-17-4, Lamivudine 135062-02-1, Repaglinide

135306-42-2, BW 1555U88 135354-02-8, Xaliproden 137234-62-9, Voriconazole 137281-23-3, Pemetrexed 137862-53-4, Valsartan 138402-11-6, Irbesartan 138531-07-4, Sinapultide 138660-96-5, Sevirumab 139264-17-8, Zolmitriptan 140207-93-8, Pentosan polysulfate sodium 141579-67-1, A 78773 141732-76-5, Exendin-4 142340-99-6, Adefovir dipivoxil 142373-60-2, Tirofiban hydrochloride 142880-36-2, Ilomastat 143201-11-0, Cerivastatin sodium 143388-64-1, Naratriptan hydrochloride 144980-29-0, Repinotan 145040-37-5, Candesartan cilexetil 145202-66-0, Rizatriptan benzoate 145258-61-3, Interferon β1 (human fibroblast protein moiety) 145375-43-5, Mitiglinide 145821-59-6, Tiagabine hydrochloride 145941-26-0, Oprelvekin 146479-72-3 147059-75-4, Trovafloxacin mesylate 147245-92-9, Glatiramer acetate 147536-97-8, Bosentan 148553-50-8, Pregabalin 148883-56-1, Tifacogin 149824-15-7, Ilodecakin 149845-06-7, Saquinavir mesylate 149950-60-7, Emivirine 151035-56-2 151063-30-8, Lisinopril-hydrochlorothiazide mixture 151319-34-5, Zaleplon 151767-02-1, Montelukast sodium 152751-57-0, Sevelamer hydrochloride 153168-05-9, Pleconaril 153259-65-5, Cilomilast 153438-49-4, Dapitant 153439-40-8, Fexofenadine hydrochloride 153773-82-1, MK 826 154039-60-8, Marimastat 154248-97-2, Imiglucerase 154361-50-9, Capecitabine 154598-52-4, Efavirenz 155141-29-0, Rosiglitazone maleate 155213-67-5, Ritonavir 156154-37-9, Losartan-hydrochlorothiazide mixture 157263-00-8, L 159282 157542-49-9, CS 834 157810-81-6, Indinavir sulfate 159989-65-8, Nelfinavir mesylate 160135-92-2 161814-49-9, Amprenavir 162011-90-7, Rofecoxib 162808-62-0, Caspofungin 164656-23-9, Dutasteride 166089-32-3, Lintuzumab 166374-48-7, CVT 124 166518-60-1, Avasimibe 169148-63-4, NN 304 169590-42-5, Celecoxib 170277-31-3, Infliximab 171228-49-2, Posaconazole 171599-83-0, Sildenafil citrate 178961-24-5, 264W94 179120-92-4, Altinicline 180288-69-1, Trastuzumab **181069-80-7**, ALT 711 181695-72-7, Valdecoxib 182167-03-9, EM 800 183547-57-1, Gantofiban 183552-38-7, Abarelix 185243-69-0, Etanercept 187348-17-0, Edodekin alfa 187523-35-9, BMS 204352 188039-54-5, Palivizumab 188062-50-2, Abacavir sulfate 188627-80-7, Eptifibatide 189013-61-4, 4030W92 192329-42-3, Prinomastat 193079-69-5, Tabimorelin 198153-51-4, Peginterferon alfa-2a 198283-73-7, ABT 594 202138-50-9, Tenofovir disoproxil fumarate 202409-33-4, Etoricoxib 205110-48-1, ABT 773 208538-73-2, FK 463 210101-16-9, Conivaptan 223652-82-2, BMS 284756 332348-12-6, BMS 188667

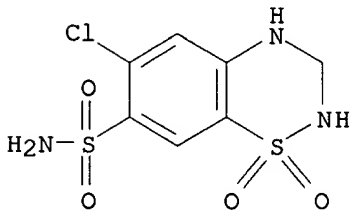
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising a polypeptide and an active agent)

IT **58-93-5**, Hydrochlorothiazide **181069-80-7**, ALT 711

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising a polypeptide and an active agent)

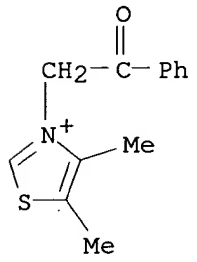
RN 58-93-5 HCAPLUS

CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-chloro-3,4-dihydro-, 1,1-dioxide (6CI, 8CI, 9CI) (CA INDEX NAME)



Delacroix

RN 181069-80-7 HCAPLUS
CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)-, bromide (9CI) (CA INDEX NAME)



L11 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the composition to the patient. The peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prepared from Glu(OBut)NCA and cephalexin hydrochloride.
2002:332011 Document Number 136:355482 Compositions comprising a polypeptide and an active agent. Piccariello, Thomas; Olon, Lawrence P.; Kirk, Randall J. (New River Pharmaceuticals, Inc., USA). PCT Int. Appl. WO 2002034237 A1 20020502, 98 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US26142 20010822. PRIORITY: US 2000-642820 20000822.
IT 50-06-6, Phenobarbital, biological studies 50-18-0, Cyclophosphamide 50-35-1, Thalidomide 50-44-2, Mercaptopurine 50-78-2, Acetylsalicylic acid 50-81-7, Vitamin C, biological studies 51-21-8, Fluorouracil 51-61-6, Dopamine, biological studies 51-63-8, Dextroamphetamine sulfate 51-98-9, Norethindrone acetate 52-01-7, Spironolactone 52-24-4, Thiotepa 52-86-8, Haloperidol 53-36-1, Methylprednisolone Acetate 54-31-9, Furosemide 55-63-0, Nitroglycerin 57-63-6, Ethinyl estradiol 58-08-2, Caffeine, biological studies 58-18-4, Methyltestosterone 58-25-3, Chlordiazepoxide 58-33-3, Promethazine hydrochloride 58-55-9, Theophylline, biological studies 58-61-7, Adenosine, biological studies **58-93-5**, Hydrochlorothiazide 59-42-7, Phenylephrine 60-54-8, Tetracycline 60-87-7, Promethazine 64-31-3, Morphine Sulfate 67-20-9, Nitrofurantoin 67-92-5, Dicyclomine hydrochloride 68-19-9, Vitamin B12 68-22-4, Norethindrone 71-58-9, Medroxyprogesterone acetate 71-68-1, Hydromorphone hydrochloride 74-79-3, Arginine, biological studies 76-41-5, Oxymorphone 76-42-6, Oxycodone 76-58-4,

Ethylmorphine 78-44-4, Carisoprodol 84-02-6, Prochlorperazine maleate 87-08-1, Penicillin V 87-33-2, Isosorbide Dinitrate 89-57-6, Mesalamine 90-82-4, Pseudoephedrine 93-14-1, Guaifenesin 113-45-1, Methylphenidate 113-52-0 113-92-8, Chlorpheniramine maleate 114-07-8, Erythromycin 124-90-3, Oxycodone hydrochloride 125-28-0, Dihydrocodeine 125-29-1, Hydrocodone 125-33-7, Primidone 125-71-3, Dextromethorphan 128-13-2, Ursodiol 129-06-6, Warfarin Sodium 132-17-2, Benzatropine methanesulfonate 132-22-9, Chlorpheniramine 143-52-2, Methyldihydromorphinone 143-71-5, Hydrocodone bitartrate 152-11-4, Verapamil hydrochloride 297-76-7, Ethynodiol diacetate 298-46-4, Carbamazepine 298-59-9, Methylphenidate hydrochloride 303-49-1, Clomipramine 315-30-0, Allopurinol 318-98-9, Propranolol Hydrochloride 378-44-9, Betamethasone 379-79-3, Ergotamine Tartrate 437-38-7, Fentanyl 439-14-5, Diazepam 446-86-6, Azathioprine 466-99-9, Hydromorphone 469-62-5, Propoxyphene 509-60-4, Dihydromorphine 514-36-3, Fludrocortisone acetate 541-15-1, Levocarnitine 549-18-8, Amitriptyline hydrochloride 554-13-2, Lithium Carbonate 561-27-3, Diacetylmorphine 595-33-5, Megestrol acetate 604-75-1, Oxazepam 630-93-3, Sodium phenytoin 657-24-9, Metformin 745-65-3, Alprostadil 747-36-4, Hydroxychloroquine sulfate 797-63-7, Levonorgestrel 846-49-1, Lorazepam 846-50-4, Temazepam 894-71-3, Nortriptyline hydrochloride 959-24-0, Sotalol hydrochloride 1134-47-0, Baclofen 1403-66-3, Gentamicin 1404-93-9, Vancomycin hydrochloride 1501-84-4, Rimantadine hydrochloride 1508-65-2, Oxybutynin chloride 1622-61-3, Clonazepam 1665-48-1, Metaxalone 1744-22-5, Riluzole 1951-25-3, Amiodarone 2078-54-8, Propofol 2152-34-3, Pemoline 2375-03-3, Methylprednisolone sodium succinate 4205-91-8 4682-36-4, Orphenadrine citrate 4759-48-2, Isotretinoin 5786-21-0, Clozapine 6202-23-9, Cyclobenzaprine hydrochloride 6493-05-6, Pentoxifylline 6533-00-2, Norgestrel 7280-37-7, Estropipate 7414-83-7, Etidronate disodium 9002-60-2, Adrenocorticotrophic hormone, biological studies 9002-69-1, Relaxin 9005-49-6, Heparin, biological studies 9014-42-0, Thrombopoietin 9039-53-6, Urokinase 9041-08-1, Dalteparin sodium 9041-92-3, .α.1-Protease inhibitor 9080-79-9, Sodium polystyrene sulfonate 10238-21-8, Glyburide 11005-12-2, β-Phytosterol 11056-06-7, Bleomycin 11140-85-5, Glucagon hydrochloride 13311-84-7, Flutamide 13614-98-7, Minocycline hydrochloride 14124-50-6, Hydrochlorothiazide-triamterene mixture 14611-52-0, Selegiline hydrochloride 14838-15-4, Phenylpropanolamine 15307-79-6, Diclofenac sodium 15663-27-1, Cisplatin 15686-71-2, Cephalexin 17140-78-2, Propoxyphene napsylate 17560-51-9, Metolazone 18559-94-9, Albuterol 19767-45-4, Mesna 20537-88-6, Amifostine 20830-75-5, Digoxin 21062-37-3D, analogs 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 22071-15-4, Ketoprofen 23031-32-5, Terbutaline sulfate 25316-40-9, Doxorubicin hydrochloride 25322-68-3, Polyethylene glycol 25332-39-2, Trazodone hydrochloride 25614-03-3, Bromocriptine 26159-34-2, Naproxen sodium 26787-78-0, Amoxicillin 27164-46-1, Cefazolin sodium 27314-97-2, Tirapazamine 28860-95-9, Carbidopa 28981-97-7, Alprazolam 29094-61-9, Glipizide 29354-16-3, Thyronine, iodo- 31677-93-7, Bupropion hydrochloride 32222-06-3, Calcitriol 32780-64-6, Labetalol hydrochloride 33069-62-4, Paclitaxel 33286-22-5, Diltiazem hydrochloride 33419-42-0, Etoposide 33564-30-6, Cefoxitin sodium 34552-83-5, Loperamide hydrochloride 34580-13-7, Ketotifen 35189-28-7, Norgestimate 36282-47-0, Tramadol hydrochloride 36505-84-7, Buspirone 36791-04-5, Ribavirin 37296-80-3, Colestipol hydrochloride 38398-32-2, Ganaxolone 41340-25-4, Etodolac 41575-94-4, Carboplatin 42200-33-9, Nadolol 42617-41-4, Activated protein C 42924-53-8, Nabumetone

49562-28-9, Fenofibrate 49842-07-1, Tobramycin sulfate 50370-12-2, Cefadroxil 50700-72-6, Vecuronium bromide 51321-79-0, Sparfosic acid 51481-61-9, Cimetidine 51773-92-3, Mefloquine hydrochloride 52232-67-4, Teriparatide 53885-35-1, Ticlopidine hydrochloride 53994-73-3, Cefaclor 54024-22-5, Desogestrel 54143-56-5, Flecainide acetate 54182-58-0, Sucralfate 54910-89-3, Fluoxetine 54965-24-1, Tamoxifen citrate 55079-83-9, Acitretin 56180-94-0, Acarbose 56238-63-2, Cefuroxime sodium 57109-90-7, Clorazepate dipotassium 57248-88-1, Pamidronate disodium 57852-57-0, Idarubicin hydrochloride 58579-51-4, Anagrelide hydrochloride 58786-99-5, Butorphanol tartrate 59122-46-2, Misoprostol 59703-84-3, Piperacillin sodium 59729-32-7, Citalopram hydrobromide 59865-13-3, Cyclosporin 59989-18-3, Eniluracil 60142-96-3, Gabapentin 60205-81-4, Ipratropium 60748-06-3, Gastrin 17 61718-82-9, Fluvoxamine maleate 62288-83-9, Desmopressin acetate 62571-86-2, Captopril 63074-08-8, Terazosin hydrochloride 63675-72-9, Nisoldipine 64221-86-9, Imipenem 64461-82-1, Tizanidine hydrochloride 64485-93-4, Cefotaxime sodium 64544-07-6, Cefuroxime axetil 65277-42-1, Ketoconazole 65646-68-6, Fenretinide 65807-02-5, Goserelin 66085-59-4, Nimodipine 66104-22-1, Pergolide 66357-35-5, Ranitidine 66722-44-9, Bisoprolol 67889-72-9, Acetaminophen-codeine phosphate mixture 67992-58-9, Sodium ioxaglate 68562-41-4, Mecasermin 68693-11-8, Modafinil 68844-77-9, Astemizole 69655-05-6, Didanosine 70458-96-7, Norfloxacin 70476-82-3, Mitoxantrone hydrochloride 72509-76-3, Felodipine 72558-82-8, Ceftazidime 72956-09-3, Carvedilol 73334-07-3, Iopromide 73573-87-2, Formoterol 73590-58-6, Omeprazole 74103-06-3, Ketorolac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising a polypeptide and an active agent)

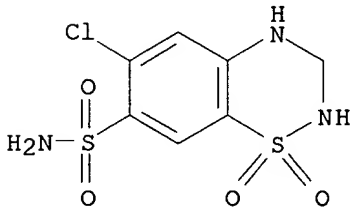
IT 74191-85-8, Doxazosin 74356-00-6, Cefotetan disodium 74381-53-6, Leuprolide acetate 74469-00-4, Amoxicillin-potassium clavulanate mixture 75330-75-5, Lovastatin 75695-93-1, Isradipine 75706-12-6, Leflunomide 75847-73-3, Enalapril 75970-99-9, Norastemizole 76470-66-1, Loracarbef 76547-98-3, Lisinopril 76584-70-8, Divalproex sodium 76820-74-1, Sodium meglumine ioxaglate 76824-35-6, Famotidine 76963-41-2, Nizatidine 78246-49-8, Paroxetine hydrochloride 78628-80-5, Terbinafine hydrochloride 78755-81-4, Flumazenil 79307-93-0, Azelastine hydrochloride 79350-37-1, Cefixime 79517-01-4, Octreotide acetate 79794-75-5, Loratadine 79902-63-9, Simvastatin 81098-60-4, Cisapride 81103-11-9, Clarithromycin 81129-83-1, Cilastatin sodium 81131-70-6, Pravastatin sodium 81409-90-7, Cabergoline 81627-83-0, M-CSF 82410-32-0, Ganciclovir 82419-36-1, Ofloxacin 82586-52-5, Moexipril hydrochloride 82586-55-8, Quinapril hydrochloride 82626-48-0, Zolpidem 82640-04-8, Raloxifene hydrochloride 82657-92-9, Prourokinase 82752-99-6, Nefazodone hydrochloride 83015-26-3, Tomoxetine 83881-52-1, Cetirizine hydrochloride 83905-01-5, Azithromycin 83928-66-9, Gepirone hydrochloride 84057-84-1, Lamotrigine 84485-00-7, Sibutramine hydrochloride 84625-61-6, Itraconazole 85650-52-8, Mirtazapine 85721-33-1, Ciprofloxacin 86050-77-3, Gadopentetate dimeglumine 86386-73-4, Fluconazole 86541-74-4, Benazepril hydrochloride 87239-81-4, Cefpodoxime proxetil 87333-19-5, Ramipril 87679-37-6, Trandolapril 90357-06-5, Bicalutamide 90566-53-3, Fluticasone 91374-20-8, Ropinirole hydrochloride 91421-42-0, Rubitecan 91832-40-5, Cefdinir 92134-98-0, Fosphenytoin sodium 92339-11-2, Iodixanol 92665-29-7, Cefprozil 93379-54-5, Esatenolol 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 95233-18-4, Atovaquone 95635-56-6, Ranolazine hydrochloride 95896-08-5, Anaritide 96036-03-2, Meropenem 96829-58-2, Orlistat

96946-42-8, Cisatracurium besylate 97240-79-4, Topiramate 97322-87-7, Troglitazone 97519-39-6, Ceftibuten 98048-97-6, Fosinopril 98319-26-7, Finasteride 98418-47-4, Metoprolol succinate 99300-78-4, Venlafaxine hydrochloride 99614-01-4, Ondansetron hydrochloride 100286-90-6, Irinotecan hydrochloride 100286-97-3, Milrinone lactate 100986-85-4, Levofloxacin 103475-41-8, Tepoxalin 103577-45-3, Lansoprazole 104227-87-4, Famciclovir 104632-25-9, Pramipexole dihydrochloride 106266-06-2, Risperidone 106392-12-5, Poloxamer 188 106861-44-3, Mivacurium chloride 107007-99-8, Granisetron hydrochloride 107753-78-6, Zafirlukast 111470-99-6, Amlodipine besylate 111974-72-2, Quetiapine fumarate 112108-01-7, Ecopipam 112529-15-4, Pioglitazone hydrochloride 112573-73-6, Ecadotril 112733-06-9, Zenarestat 113427-24-0, Epoetin alfa 114977-28-5, Docetaxel 115956-13-3, Dolasetron mesylate 116539-59-4, Duloxetine 117976-90-6, Rabeprazole sodium 118390-30-0, Interferon alfacon-1 119302-91-9, Rocuronium bromide 119413-54-6, Topotecan hydrochloride 120011-70-3, Donepezil hydrochloride 120066-54-8, Gadoteridol 120202-66-6, Clopidogrel bisulfate 120511-73-1, Anastrozole 120635-74-7, Cilansetron 121032-29-9, Nelarabine 121181-53-1D, PEGylated 121584-18-7, Valspodar 122111-03-9, Gemcitabine hydrochloride 123122-55-4, Candoxatril 123258-84-4, Itasetron 124584-08-3, Nesiritide 124750-99-8, Losartan potassium 124832-27-5, Valacyclovir hydrochloride 124937-52-6, Tolterodine tartrate 125317-39-7, Vinorelbine tartrate 126544-47-6, Ciclesonide 127254-12-0, Sitafloxacin 127779-20-8, Saquinavir 128298-28-2, Remacemide 128794-94-5, Mycophenolate mofetil 129318-43-0, Alendronate sodium 129580-63-8, Satraplatin 129618-40-2, Nevirapine 129722-12-9, Aripiprazole 130018-77-8, Levocetirizine 130325-35-8, PD 135158 131918-61-1, Paricalcitol 132449-46-8, Lesopitron 132539-06-1, Olanzapine 133107-64-9, Insulin lispro 133737-32-3, Pagoclone 134523-03-8, Atorvastatin calcium 134564-82-2, Befloxatone 134678-17-4, Lamivudine 135062-02-1, Repaglinide 135306-42-2, BW 1555U88 135354-02-8, Xaliproden 137234-62-9, Voriconazole 137281-23-3, Pemetrexed 137862-53-4, Valsartan 138402-11-6, Irbesartan 138531-07-4, Sinapultide 138660-96-5, Sevirumab 139264-17-8, Zolmitriptan 140207-93-8, Pentosan polysulfate sodium 141579-67-1, A 78773 141732-76-5, Exendin-4 142340-99-6, Adefovir dipivoxil 142373-60-2, Tirofiban hydrochloride 142880-36-2, Ilomastat 143201-11-0, Cerivastatin sodium 143388-64-1, Naratriptan hydrochloride 144980-29-0, Repinotan 145040-37-5, Candesartan cilexetil 145202-66-0, Rizatriptan benzoate 145258-61-3, Interferon β1 (human fibroblast protein moiety) 145375-43-5, Mitiglinide 145821-59-6, Tiagabine hydrochloride 145941-26-0, Oprelvekin 146479-72-3 147059-75-4, Trovafloxacin mesylate 147245-92-9, Glatiramer acetate 147536-97-8, Bosentan 148553-50-8, Pregabalin 148883-56-1, Tifacogin 149824-15-7, Ilodecakin 149845-06-7, Saquinavir mesylate 149950-60-7, Emivirine 151035-56-2 151063-30-8, Lisinopril-hydrochlorothiazide mixture 151319-34-5, Zaleplon 151767-02-1, Montelukast sodium 152751-57-0, Sevelamer hydrochloride 153168-05-9, Pleconaril 153259-65-5, Cilomilast 153438-49-4, Dapitant 153439-40-8, Fexofenadine hydrochloride 153773-82-1, MK 826 154039-60-8, Marimastat 154248-97-2, Imiglucerase 154361-50-9, Capecitabine 154598-52-4, Efavirenz 155141-29-0, Rosiglitazone maleate 155213-67-5, Ritonavir 156154-37-9, Losartan-hydrochlorothiazide mixture 157263-00-8, L 159282 157542-49-9, CS 834 157810-81-6, Indinavir sulfate 159989-65-8, Nelfinavir mesylate 160135-92-2 161814-49-9, Amprenavir 162011-90-7, Rofecoxib 162808-62-0, Caspofungin 164656-23-9, Dutasteride 166089-32-3, Lintuzumab 166374-48-7, CVT 124

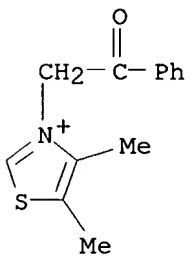
166518-60-1, Avasimibe 169148-63-4, NN 304 169590-42-5, Celecoxib 170277-31-3, Infliximab 171228-49-2, Posaconazole 171599-83-0, Sildenafil citrate 178961-24-5, 264W94 179120-92-4, Altinicline 180288-69-1, Trastuzumab **181069-80-7**, ALT 711 181695-72-7, Valdecoxib 182167-03-9, EM 800 183547-57-1, Gantofiban 183552-38-7, Abarelix 185243-69-0, Etanercept 187348-17-0, Edodekin alfa 187523-35-9, BMS 204352 188039-54-5, Palivizumab 188062-50-2, Abacavir sulfate 188627-80-7, Eptifibatide 189013-61-4, 4030W92 192329-42-3, Prinomastat 193079-69-5, Tabimorelin 198153-51-4, Peginterferon alfa-2a 198283-73-7, ABT 594 202138-50-9, Tenofovir disoproxil fumarate 202409-33-4, Etoricoxib 205110-48-1, ABT 773 208538-73-2, FK 463 210101-16-9, Conivaptan 223652-82-2, BMS 284756 332348-12-6, BMS 188667
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising a polypeptide and an active agent)

IT **58-93-5**, Hydrochlorothiazide **181069-80-7**, ALT 711
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising a polypeptide and an active agent)

RN 58-93-5 HCAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-chloro-3,4-dihydro-, 1,1-dioxide (6CI, 8CI, 9CI) (CA INDEX NAME)



RN 181069-80-7 HCAPLUS
CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)-, bromide (9CI) (CA INDEX NAME)



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